REMARKS/ARGUMENTS

Status of the Claims

Upon entry of the present amendment, claims 1, 3-5, 17-25, 28-29, 31, 36, 43-45, 49 and 77 are pending. Claims 1, 3-4, 7 and 36 are under examination. Claims 5, 17-25, 28-29, 31, 43-45 and 49 are withdrawn as directed to non-elected inventions. Claims 1 and 36 are amended. New claim 77 is added.

Claim 1 is amended to set forth the CGX-2 function of promoting cell proliferation and binding to MGC10334 and/or CENPC1. Support is found, for example, on page 52, lines 22-24; on page 73, lines 23-29, and throughout the specification.

Claim 36 is amended for proper antecedent basis.

New claim 77 sets forth the language of claim 1(a).

The amendments are made to place the claims in form for allowance or to reduce issues for appeal. No new matter is added by the present amendments and the Examiner is respectfully requested to enter them.

Telephonic Interview

The Examiner and her supervisor are thanked for graciously granting the telephonic interview of October 16, 2007. The issues discussed are as set forth in the pending Office Action and in the present response.

Rejection under 35 U.S.C. 112, second paragraph

Claims 1, 3-4, 7, and 36 stand rejected under 35 U.S.C. § 112, second paragraph for allegedly failing to particularly point out and distinctly claim the subject matter regarded as the invention. In particular, the Examiner objects to the recitation of "cell proliferative activity" in claim 1. The Examiner also alleges that claim 36 is unclear.

Applicants do not agree with the Examiner. However, in the interest of furthering prosecution, Applicants have (i) amended claim 1 to specify that the protein at issue has the ability to promote cell proliferation and (ii) amended claim 36 in accordance with the Examiner's

suggestion, to specify that the claimed reagent binds to a CGX-2 polynucleotide as defined in claim 1. Accordingly, reconsideration and withdrawal of the outstanding indefiniteness rejection is respectfully requested.

Rejection under 35 U.S.C. 112, first paragraph, written description

Claims 1, 3-4, and 7 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with the written description requirement. This rejection is respectfully traversed.

The Examiner alleges that the claims encompass subject matter which was not described in the specification in such a way as to convey possession of the claimed invention. Specifically, the Examiner alleges conception of a broad genus, composed of potentially highly diverse functions, such as that presently claimed, cannot be achieved until an actual reduction to practice has occurred, regardless of the complexity or simplicity of the isolation method. Moreover, the Examiner alleges in that only experimental research can confirm the artisan's best guess as to the function of the structurally related protein, adequate written description requires disclosure of the sequence itself.

Applicants respectfully disagree with the Examiner's position. Applicants maintain that the Examiner's absolute requirement for actual reduction to practice of exemplary sequences in order demonstrate possession of the claimed invention is in conflict with the statutory requirements as well as the USPTO's own written description guidelines.

It is well accepted that a specification may, within the meaning of 35 U.S.C. 112, first paragraph, contain a written description of a broadly claimed invention ***without*** reducing to practice each and every species encompassed by the claims. In fact, the law does not even require that the specification describe the exact details for ***preparing every species*** within a claimed genus, much less the actual construction of the species themselves. Moreover, even if the Examiner considers the subject matter of the claims to be broader than that disclosed in the original specification, the written description requirement may be satisfied if the broader concept would naturally occur to one skilled in the art upon reading the earlier specification.

It is further well settled that possession of a genus may be satisfied through sufficient description of a "representative number of species" by: (a) an actual reduction to practice, (b) a reduction to drawings, or (c) disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlation between function and structure, or by a combination of such identifying characteristics sufficient to show the applicant was in possession of the claimed genus. In other words, possession of a genus can be evidenced by describing the distinguishing identifying characteristics common to the divergent species encompassed. *See*, M.P.E.P. § 2163.02.

In this context, a "representative number of species" means that the species which are actually described are representative of the entire genus. Thus, when there is substantial variation with the genus, one must describe a sufficient variety of species to reflect the variation. What constitutes a representative number is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a representative number of species depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed.

In this case, the claims encompass sequence variants of SEQ ID NO: 12 (claim 1(b)) and hybridizing homologs of SEQ ID NO: 11 (claim 1(c)). In both cases, the members of the claimed genus are expressly defined both in terms of structure (*e.g.*, at least 95% identical) and function (*e.g.*, encoding a polypeptide that promotes cell proliferation and binds to MGC10334 and/or CENPC1). Applicants submit that one skilled in the art would expect the claimed genera to have only limited variation. To that end, the Examiner's attention is respectfully directed to Examples 9 and 14 of the Training Materials accompanying the Revised Interim Written Description Guidelines published January 5, 2001 ("Written Description Training Materials," *see*, http://www.uspto.gov/web/menu/written.pdf).

Example 14 of the Training Materials analyzes a claim directed to variants of a protein that are *at least 95% identical to a particular disclosed sequence and that have a*

particularly specified activity. Therein, the PTO concludes that "the genus of proteins that must be variants. . .*does not have substantial variation* since all the variants must possess the specific catalytic activity and must have at least 95% identity to the reference sequence", a finding which directly conflicts with the Examiner's suggestion that the phrase "95% sequence identity" encompasses a "broad genus" having "highly diverse functions."

Example 14 goes on to state that "the single species disclosed is representative of the genus because all members have at least 95% structural identity with the reference compound and because of the presence of an assay which applicant provides for identifying all of the at least 95% identical variants...which are capable of the specified catalytic activity." Accordingly, "one skilled in the art would conclude that applicant was in possession of the necessary common attributes possessed by the members of the genus" (i.e., the example claim meets the written description requirement of 35 USC § 112, first paragraph). *See*, Written Description Training Materials at pages 53-55.

Applicants' amended claim 1(b) is analogous to the claim of Example 14 in that it is directed to an isolated nucleic acid encoding a protein having (a) a specifically identified structure, namely at least 95% identity to SEQ ID NO: 12, and (b) a specifically identified function, namely the promotion of cell proliferation and binding to MGC10334 and/or CENPC1. As discussed above, since the species are defined both in terms of specific structure and specific function, the genus of nucleotides encompassed by the claim would not be expected to be substantially variable. Thus, it follows that since the genus is not widely variable, a single species—namely, the DNA of SEQ ID NO: 11—is sufficient to demonstrate possession.

Furthermore, Applicants' specification sets forth assays for preparing and identifying such variants capable of performing the specified function. *See*, for example, page 52, lines 24-27; page 73, lines 23-29 and Example 4 (assaying the ability of a protein, particularly an NFXL1 protein, to promote cell proliferation, and to bind to MGC10334 and/or CENPC1); page 54, line 19 to p. 56, line 7 (introducing mutations); page 49, lines 19-32 (determining percent identity). Accordingly, Applicants submit that the instant specification provides an adequate written description of the genus of sequence variants encompassed by

claim 1(b) so as to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the invention now claimed.

Regarding claim 1(c), the Examiner's attention is respectfully directed to Example 9 of the Written Description Training Materials. Applicants submit that allowance of claim 1 is in line with USPTO policy. Specifically, Example 9 analyzes a claim directed to an isolated nucleic acid that hybridizes to a particular disclosed sequence and encodes a protein having a particularly specified activity. Therein, the PTO concludes that "a person of skill in the art *would not expect substantial variation among species* encompassed within the scope of the claims because the *highly stringent hybridization conditions set forth in the claims yield structurally similar DNAs*.[1] In light of the highly stringent hybridization conditions in combination with the requisite function of the DNA and the level of skill and knowledge in the art, a single species is sufficient to demonstrate possession of the claimed genus. Accordingly, claim 1 of Example 9 was determined to be adequately described (*i.e.*, to meet the written description requirement of 35 USC § 112, first paragraph). *See*, Written Description Training Materials at pages 36-37.

Applicants' claim 1(c) as amended herein, is analogous to claim 1 of Example 9 in that it expressly specifies hybridization under specifically defined "stringent conditions" and requires the resulting DNA to have a specifically identified function, namely the ability to promote cell proliferation and to bind to MGC10334 and/or CENPC1. As discussed above, one would not expect substantial variation among species included within the scope of the claims because the highly stringent hybridization conditions set forth in the claims yield structurally similar DNAs. Thus, it follows that since the genus is not widely variable, a single species is sufficient to demonstrate possession.

Furthermore, Applicants' specification explicitly sets forth assays for selecting such hybridizing nucleic acids. *See*, for example, page 52, lines 24-27; page 73, lines 23-29 and

[1] We note that Example 9 defines highly stringent hybridization conditions as "6X SSC and 65 °C". The instant claims require an even greater stringency, specifying not only 6X SSC, 65 °C, but also specific reactants (50 mM Tris-HCl at pH 7.5, 1 mM EDTA, 0.02% PVP, 0.02% Ficoll, 0.02% BSA, and 500 mg/ml denatured salmon sperm)

Example 4 (assaying the ability of a protein, particularly an NFXL1 protein, to promote cell proliferation, and to bind to MGC10334 and/or CENPC1); and page 52, line 32 to page 54, line 17 (hybridization techniques). Accordingly, we submit that the instant specification provides an adequate written description of the genus of hybridizing DNA homologs encompassed by claim 1(c) so as to convey with reasonable clarity to those skilled in the art that, as of the filing date sought, Applicants were in possession of the invention now claimed.

The facts of the present claims and specification are like those at issue in *Ex parte* Bandman (BPAI Appeal No. 2004-2319) ("Bandman") and *Ex parte* Sun (BPAI Appeal No. 2003-1993) ("Sun"). In Bandman, claims directed to an isolated polynucleotide encoding a polypeptide comprising an amino acid sequence at least 95% identical to a recited SEQ ID NO were rejected by an Examiner as failing to comply with the written description and enablement requirements. The Examiner alleged that the specification only provided a single species, and did not provide any disclosure of any particular structure to function/activity relationship in the single disclosed species. *See*, page 3 of the Bandman Decision. The specification in Bandman disclosed the complete structure of the polypeptide of the recited SEQ ID NO and a polynucleotide encoding it. The claims at issue in Bandman did not recite a function of the encoded protein. *See*, page 1 of the Bandman Decision.

In Sun, claims directed to an isolated polynucleotide at least 80% identical to a recited SEQ ID NO were rejected by an Examiner as failing to comply with the written description and enablement requirements. The Examiner alleged that the specification does not set forth what specific structural or physical features define the claimed isolated nucleic acids. The Examiner alleged that the skilled person could not predict the structure and function of isolated nucleic acid having at least 80% sequence identity to the recited SEQ ID NO. *See*, page 7 of the Sun Decision. The specification in Sun disclosed the complete structure of the polynucleotide of the recited SEQ ID NO, and the encoded polypeptide. The claims at issue in Sun also did not recite a function of the encoded protein. *See*, pages 1-2 of the Sun Decision.

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and specific wash conditions (0.2X SSC, 0.01% BSA at 50 °C). Accordingly, one of skill would expect the instantly claimed hybridizing homologs to possess even less variability.

The BPAI reversed the Examiner's rejections under 35 U.S.C. § 112, first paragraph, in both Bandman and Sun, in each case stating that the specification described the complete sequence of the recited sequence and the genus limited to polypeptides or polynucleotides comprising 95% or 80% sequence identity to the recited SEQ ID NO. The BPAI noted that the Examiner had not adequately explained and/or provided evidence to support the assertion that the specification did not provide any disclosure of any particular structure to function/activity relationship in the single disclosed species. *See*, page 4 of the Bandman Decision and pages 7-10 of the Sun Decision.

Here, the claims are directed to isolated DNA encoding a polypeptide that structurally shares at least about 95% amino acid sequence identity with the recited sequence (*i.e.*, SEQ ID NO:12) ***and*** has the function of promoting cell proliferation and binding to MGC10334 and/or CENPC1. In comparison to the claims in Bandman and Sun, the presently claimed isolated DNAs encompass a more limited scope for the recited polypeptide and polynucleotide because the present claims require a particular function of the polypeptide. Moreover, the Examiner has not explained and/or provided evidence to support the assertion that the specification does not provide any disclosure of any particular structure to function/activity relationship in the single disclosed species. In fact, Applicants teach that the predicted NFXL1 protein contains a ring finger domain (codons 160-219), 12 NFX type Zn-finger domains (codons 265-794), a coiled coil region (codons 822-873), and a transmembrane region (codons 889-906) and is further known to associate with MGC10334 and CENPC1. *See*, page 8, lines 18-27 and Figure 9b of the present specification.

In summary, given the specifically enumerated restrictions on both the structure and function of the claimed polynucleotides, Applicants respectfully submit that one would not expect substantial variability to exist within the claimed genera and, as such, would find the representative species disclosed in the instant specification to be sufficient to demonstrate possession of the claimed invention. Accordingly, reconsideration and withdrawal of the outstanding written description rejection in view of the amendments and remarks are respectfully requested.

Rejection under 35 U.S.C. 112, first paragraph, enablement

Claims 1, 3-4, and 7 stand rejected under 35 U.S.C. § 112, first paragraph, for allegedly failing to comply with enablement requirement. Applicants respectfully traverse.

The Examiner alleges that the specification fails to provide guidance regarding which structural domains need to be retained in the protein to maintain the functional activity of the protein, and that undue experimentation would be required to identify the particular residues of the protein that could be modified or mutated without affecting the requisite cell proliferative activity.

Applicant's respectfully disagree with the Examiner's position. Applicants respectfully submit that the Examiner's requirement for specific instructional guidance and reduction to practice of exemplary embodiments is in conflict with the USPTO's own enablement guidelines. Specifically, the "Training Materials For Examining Patent Applications With Respect To 35 USC § 112, First Paragraph - Enablement Chemical/Biotechnical Applications"[2] sets forth an enablement decision tree that first asks the question: "Does the specification teach how to make and use at least one embodiment encompassed by the claims as a whole without undue experimentation?" A note to the question states that "if there is a working example, the answer to the question cannot be 'NO'." Herein, Applicants not only provide general guidance as to how to make and use embodiments of the claimed invention (see, for example, pages 46 to 58) but also describe at least one representative species that falls within the scope of the claimed invention (i.e., SEQ ID NO: 11). Accordingly, the answer to the first question is necessarily "YES".

The second question in the enablement decision tree is: "Are the enabled embodiments representative of the full scope of the claim?" As discussed above, the USPTO itself has deemed a single disclosed species to be representative of the claimed genus of hybridizing homologs and sequence variants encompassed by the instant claims. Specifically, the high degree of sequence identity and/or the highly stringent hybridizing techniques required

[2] Enablement Training Materials are found at http://www.uspto.gov/web/offices/pac/dapp/1pecba.htm.

by the claims, coupled with the specified restriction on function, results in a genus of structurally similar nucleotides. Accordingly, a person of skill in the art would not expect substantial variation among species within the genus. In that Applicants have disclosed at least one representative species (i.e., SEQ ID NO: 11), the answer to this second question is necessarily "YES".

Thus, following the guidelines of the enablement decision tree, Applicants respectfully submit that no enablement rejection should be made under these circumstances. Accordingly, Applicants submit that the enablement rejection of the present claims is in error.

Furthermore, as for the Examiner's suggestion that without specific guidance as to which amino acids may be mutated, the experimentation left to those skilled in the art is undue, it is important to remember that the test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, provided it is merely routine. *See, In re Wands* 8 U.S.P.Q. 1400, 1404 (Fed. Cir. 1988). In this case, "trial and error" testing needed to identify regions of the protein that can tolerate mutation is within the parameters of routine experimentation and optimization.

Moreover, contrary to the Examiner's assertion, Applicants have indeed provided guidance as to structural domains associated with functional activity, noting that the predicted NFXL1 protein contains a ring finger domain (codons 160-219), 12 NFX type Zn-finger domains (codons 265-794), a coiled coil region (codons 822-873), and a transmembrane region (codons 889-906) and is further known to bind to MGC10334 and/or CENPC1. *See*, page 8, lines 18-27 and Figure 9b. Following this guidance, one skilled in the art would expect those regions outside the designated domains to be most tolerant of variation.

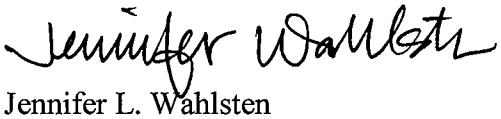
In view of the foregoing, Applicants respectfully submit that one skilled in the art could make or use the claimed invention from the disclosures in the specification, coupled with information known in the art, without undue experimentation. Accordingly, reconsideration and withdrawal of the outstanding enablement rejection in view of the amendments and remarks herein are respectfully requested.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance and an action to that end is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,



Jennifer L. Wahlsten
Reg. No. 46,226

TOWNSEND and TOWNSEND and CREW LLP
Two Embarcadero Center, Eighth Floor
San Francisco, California 94111-3834
Tel: 415-576-0200
Fax: 415-576-0300
Attachments
JLW:jlw
61177515 v1